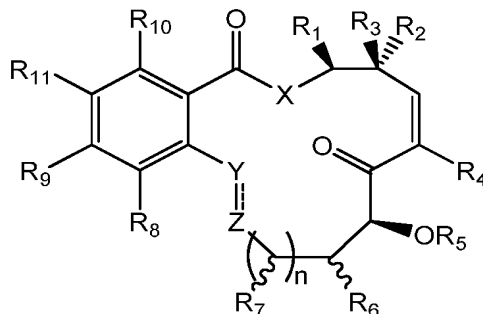


**AMENDMENTS TO THE CLAIMS**

1. (previously presented) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester thereof; wherein

R<sub>1</sub> is hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl;

R<sub>2</sub> is C<sub>1-6</sub> alkyl;

R<sub>3</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, or a C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl moiety;

or

R<sub>1</sub> and R<sub>3</sub>, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R<sub>4</sub> is hydrogen or halogen;

R<sub>5</sub> is hydrogen or an oxygen protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or a C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl or C<sub>2</sub>-C<sub>20</sub> alkynyl moiety optionally substituted with hydroxyl, protected hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;

R<sub>9</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, OR<sub>12</sub>, SR<sub>12</sub>, NR<sub>12</sub>R<sub>13</sub>, -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>;

wherein R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl; or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X<sub>1</sub> and X<sub>2</sub> are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X<sub>2</sub>-R<sub>14</sub> together are N<sub>3</sub> or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R<sub>14</sub> is hydrogen, or an C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, C<sub>1</sub>-C<sub>20</sub>alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or C<sub>1</sub>-C<sub>20</sub>alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl moiety, or is -(C=O)NHR<sub>15</sub>, -(C=O)OR<sub>15</sub>, or -(C=O)R<sub>15</sub>, wherein each occurrence of R<sub>15</sub> is independently hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl; or R<sub>14</sub> is -SO<sub>2</sub>(R<sub>16</sub>), wherein R<sub>16</sub> is a C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl or C<sub>2</sub>-C<sub>20</sub> alkynyl moiety, wherein one or more of R<sub>14</sub>, R<sub>15</sub>, or R<sub>16</sub> are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R<sub>8</sub> and R<sub>9</sub> may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with

hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R<sub>10</sub> is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R<sub>11</sub> is hydrogen, hydroxyl or protected hydroxyl;

X is O;

Y is CHR<sub>17</sub>, C=O, or CR<sub>17</sub>; and Z is CHR<sub>18</sub>, C=O, or CR<sub>18</sub>, wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is independently hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl or C<sub>2</sub>-C<sub>20</sub> alkynyl wherein Y and Z may be connected by a single or double bond;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyl dimethylsilyl ether, tribenzyl silyl ether, t-butyl diphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and wherein C<sub>3</sub>-C<sub>14</sub> heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

2. (previously presented) The composition of claim 1, wherein:

R<sub>1</sub> is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R<sub>2</sub> is methyl;

R<sub>3</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R<sub>1</sub> and R<sub>3</sub>, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R<sub>4</sub> is hydrogen or halogen;

R<sub>5</sub> is hydrogen or a protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;

R<sub>9</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, OR<sub>12</sub>, SR<sub>12</sub>, NR<sub>12</sub>R<sub>13</sub>, -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>;

wherein R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, lower alkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X<sub>1</sub> and X<sub>2</sub> are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X<sub>2</sub>-R<sub>14</sub> together are N<sub>3</sub> or are a saturated or unsaturated heterocyclic moiety, p is 2-10, and

R<sub>14</sub> is hydrogen, or a C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl moiety, or is -(C=O)NHR<sub>15</sub>, -(C=O)OR<sub>15</sub>, or -(C=O)R<sub>15</sub>, wherein each occurrence of R<sub>15</sub> is independently hydrogen, alkyl, heteroalkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or R<sub>14</sub> is -SO<sub>2</sub>(R<sub>16</sub>), wherein R<sub>16</sub> is an alkyl moiety, wherein one or more of R<sub>14</sub>, R<sub>15</sub>, or R<sub>16</sub> are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R<sub>8</sub> and R<sub>9</sub> may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with

hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

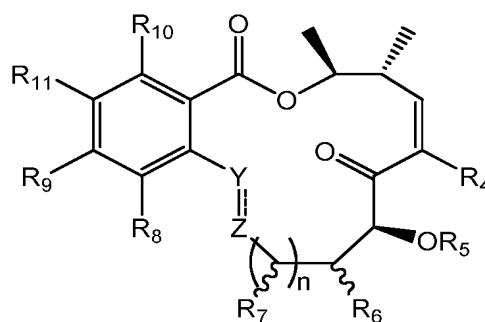
R<sub>10</sub> is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R<sub>11</sub> is hydrogen, hydroxyl or protected hydroxyl;

X is O;

Y is CHR<sub>17</sub>, C=O, or CR<sub>17</sub>; and Z is CHR<sub>18</sub>, C=O, or CR<sub>18</sub>, wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is independently hydrogen or lower alkyl, wherein Y and Z may be connected by a single or double bond.

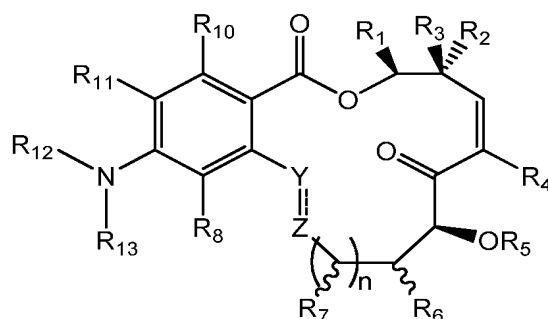
3. (currently amended) The composition of claim 2, where ~~and~~ n is 1.
4. (original) The composition of claim 2, where R<sub>4</sub> is halogen.
5. (original) The composition of claim 2, where R<sub>4</sub> is fluorine.
6. (original) The composition of claim 2, where Y and Z together represent -CH=CH-.
7. (original) The composition of claim 2, where Y and Z together represent trans -CH=CH-.
8. (previously presented) The composition of claim 2, wherein R<sub>1</sub> and R<sub>2</sub> are each methyl and R<sub>3</sub> is hydrogen and the compound has the structure:



wherein R<sub>4</sub>-R<sub>11</sub>, n, Y and Z are as defined in claim 2.

9. (previously presented) The composition of claim 8, wherein n is 1.
10. (original) The composition of claim 8, wherein R<sub>4</sub> is halogen.

11. (original) The composition of claim 8, wherein Y and Z together represent  $-\text{CH}=\text{CH}-$ .
12. (previously presented) The composition of claim 8, wherein n is 1,  $\text{R}_4$  is halogen and Y and Z together represent  $-\text{CH}=\text{CH}-$ .
13. (original) The composition of claim 11 or 12 wherein  $-\text{CH}=\text{CH}-$  is trans.
14. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester thereof; wherein

$\text{R}_1$  is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or  $\text{C}_3\text{-C}_{14}$  aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

$\text{R}_2$  is  $\text{C}_{1-6}$  alkyl;

$\text{R}_3$  is hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or  $\text{C}_3\text{-C}_{14}$  aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

$\text{R}_1$  and  $\text{R}_3$ , when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

$\text{R}_4$  is hydrogen or halogen;

$\text{R}_5$  is hydrogen or a protecting group;

$\text{R}_6$  is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;  
R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;  
R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, lower alkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

R<sub>10</sub> is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R<sub>11</sub> is hydrogen, hydroxyl or protected hydroxyl;

~~X~~ is O;

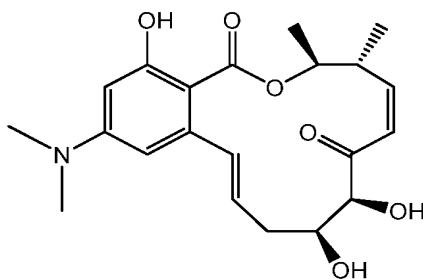
Y is CHR<sub>17</sub>, C=O, or CR<sub>17</sub>; and Z is CHR<sub>18</sub>, C=O, or CR<sub>18</sub>, wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is independently hydrogen or lower alkyl, wherein Y and Z may be connected by a single or double bond, or

R<sub>13</sub> and R<sub>8</sub> may, when taken together, form a cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilylether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

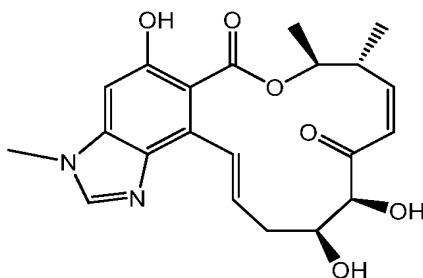
wherein C<sub>3</sub>-C<sub>14</sub> heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

15. (previously presented) The composition of claim 14, wherein  $n$  is 1.
16. (original) The composition of claim 14, wherein  $R_4$  is halogen.
17. (original) The composition of claim 14, wherein  $Y$  and  $Z$  together represent  $-\text{CH}=\text{CH}-$ .
18. (original) The composition of claim 14, wherein  $R_1$  and  $R_2$  are each methyl and  $R_3$  is hydrogen.
19. (previously presented) The composition of claim 14, wherein  $n$  is 1,  $R_1$  and  $R_2$  are each methyl,  $R_3$  is hydrogen,  $R_4$  is halogen, and  $Y$  and  $Z$  together represent  $-\text{CH}=\text{CH}-$ .
20. (original) The composition of claim 17 or 19, wherein  $-\text{CH}=\text{CH}-$  is trans.
- 21-22. (cancelled)
23. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

24. (previously presented) The composition of claim 14, wherein the compound has the structure:

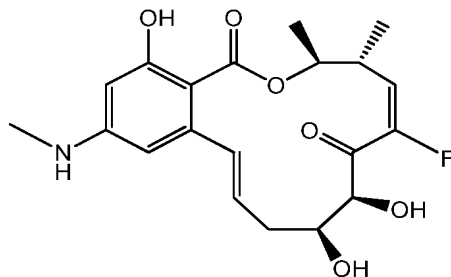




or a pharmaceutically acceptable salt or ester thereof.

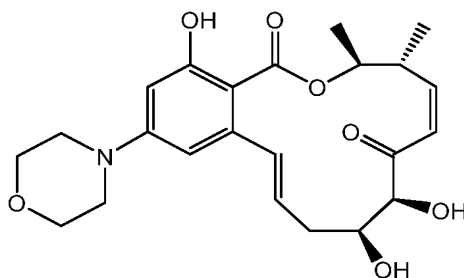
25-26. (cancelled)

27. (previously presented) The composition of claim 14, wherein the compound has the structure:



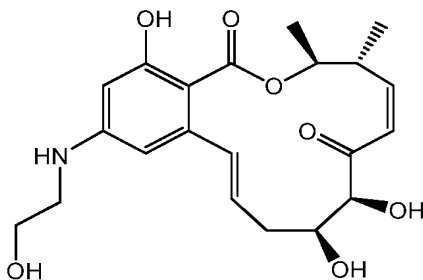
or a pharmaceutically acceptable salt or ester thereof.

28. (previously presented) The composition of claim 14, wherein the compound has the structure:



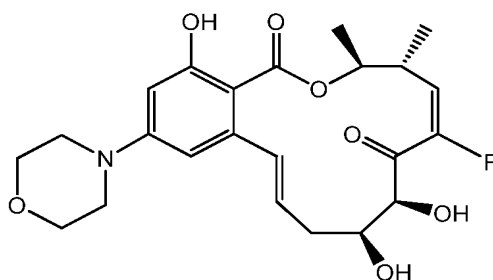
or a pharmaceutically acceptable salt or ester thereof.

29. (previously presented) The composition of claim 14, wherein the compound has the structure:



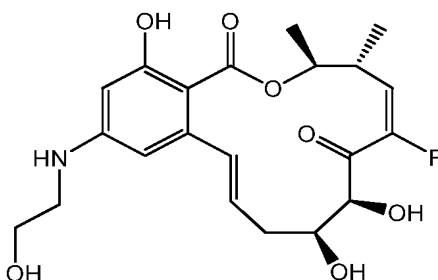
or a pharmaceutically acceptable salt or ester thereof.

30. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

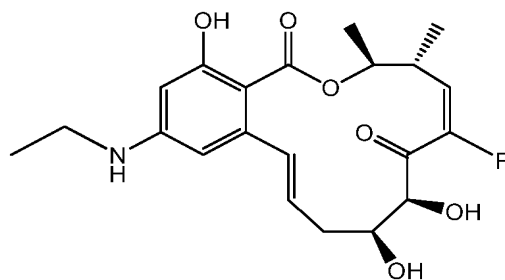
31. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

32. (cancelled)

33. (previously presented) The composition of claim 14, wherein the compound has the structure:

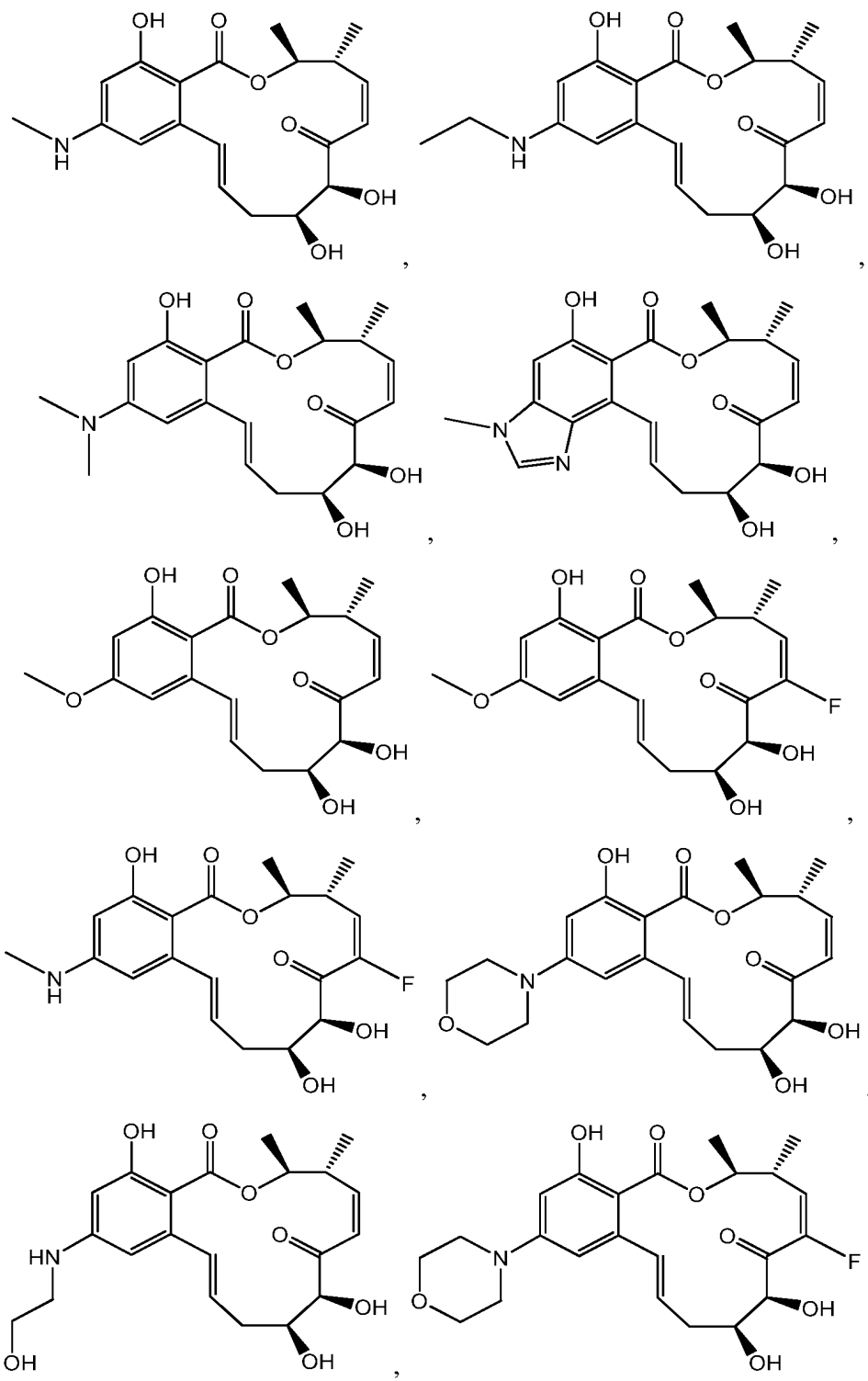


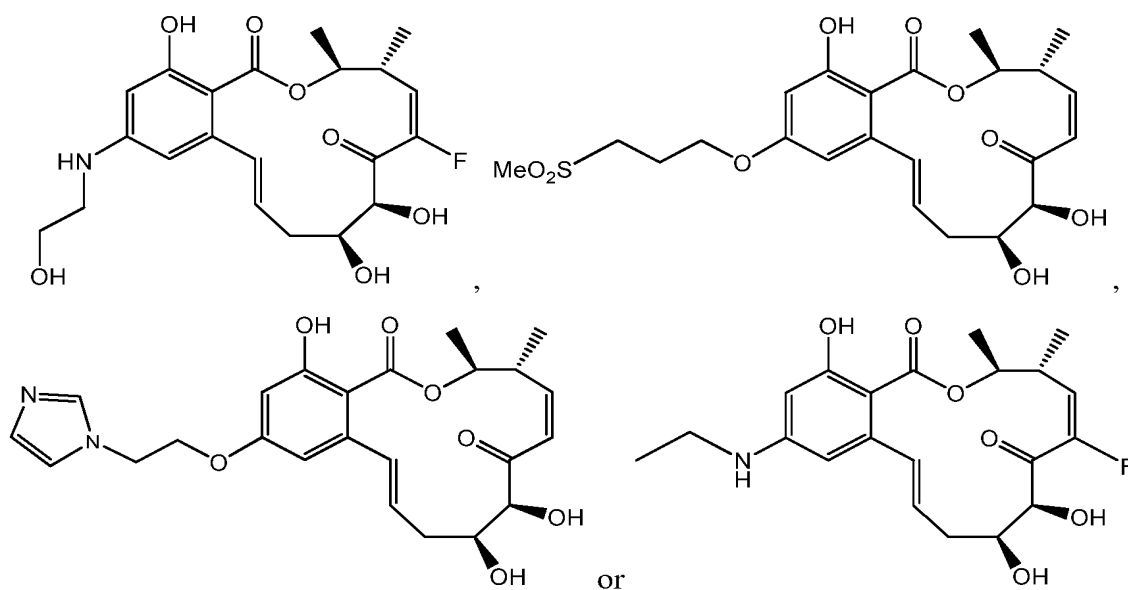
or a pharmaceutically acceptable salt or ester thereof.

- 34-35. (cancelled)

36. (withdrawn) The pharmaceutical composition of claim 1, wherein the composition is for oral administration.
37. (cancelled)
38. (withdrawn) The pharmaceutical composition of claim 1, wherein the compound is present in an amount effective to inhibit production of a pro-inflammatory and/or immunologic cytokine selected from the group consisting of TNF $\alpha$ , IL-1, IL-6, IL-8 and IL-2.
39. (withdrawn) A method for treating rheumatoid arthritis, psoriasis, asthma, sepsis, inflammatory bowel disease, atopic dermatitis or Crohn's disease comprising the step of systemically administering to a subject in need thereof a therapeutically effective amount of a pharmaceutical composition of claim 1.
40. (withdrawn) The method of claim 39, wherein the compound is administered orally.
41. (cancelled)
42. (withdrawn) The method of claim 39, wherein the method is for treating psoriasis.

43. (withdrawn) The method of claim 39, wherein the compound has any one of the following structures:





or pharmaceutically acceptable salt or ester thereof.

44-45. (cancelled)

46. (withdrawn) The composition of claim 2, where  $R_1$  is hydrogen or methyl.

47. (withdrawn) The composition of claim 2, where  $R_3$  is hydrogen or halogen.

48. (withdrawn) The composition of claim 2, where  $R_4$  is hydrogen.

49. (withdrawn) The composition of claim 2, where  $R_5$  is hydrogen.

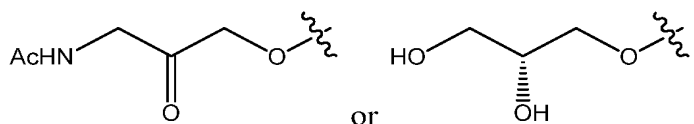
50. (withdrawn) The composition of claim 2, where  $R_6$  is hydroxyl.

51. (withdrawn) The composition of claim 2, where  $R_7$  is hydrogen or hydroxyl.

52. (withdrawn) The composition of claim 2, where  $R_8$  is hydrogen or halogen.

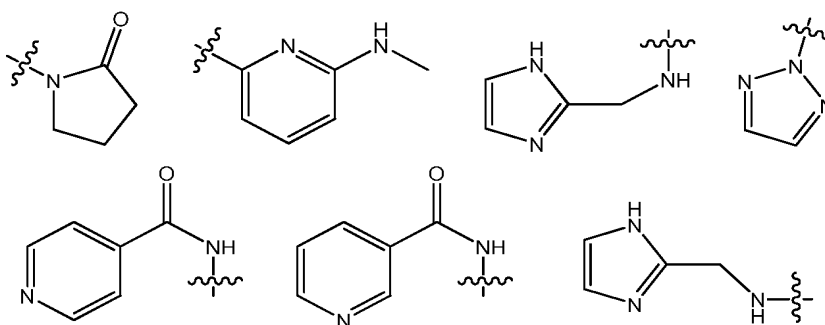
53. (withdrawn) The composition of claim 2, where  $R_9$  is hydroxyl, protected hydroxyl, - $OR_{12}$ , - $NR_{12}R_{13}$ , or - $O(CH_2)_pX_2-R_{14}$ , wherein  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$  and  $X_2$  are as defined in claim 2.

54. (withdrawn) The composition of claim 53, where  $R_9$  is  $-OR_{12}$ , wherein  $R_{12}$  is methyl, ethyl, propyl, isopropyl, butyl,  $-CH_2COOMe$ , Bn, PMB (MPM), 3,4-CIBn, or  $R_9$  is



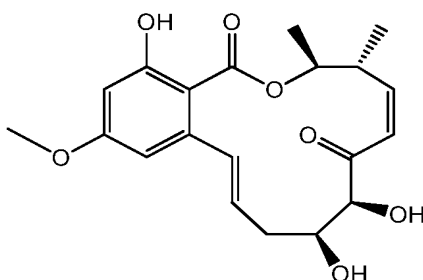
55. (withdrawn) The composition of claim 53, where  $R_9$  is  $-NR_{12}R_{13}$ , or wherein  $R_{12}$  is methyl, ethyl, propyl, isopropyl, or butyl, optionally substituted with one or more occurrences of hydroxyl or protected hydroxyl, and  $R_{13}$  is hydrogen or lower alkyl, or  $NR_{12}R_{13}$  together represents a 5- or 6- membered heterocyclic moiety.

56. (withdrawn) The composition of claim 53, where  $R_9$  is  $-O(CH_2)_pX_2-R_{14}$ , wherein  $X_2-R_{14}$  together represent  $N_3$ ,  $NMe_2$ ,  $NHAc$ ,  $NHSO_2Me$ ,  $NHCONHMe$ ,  $NHCONHPh$ , morpholine, imidazole, aminopyridine, or any one of:



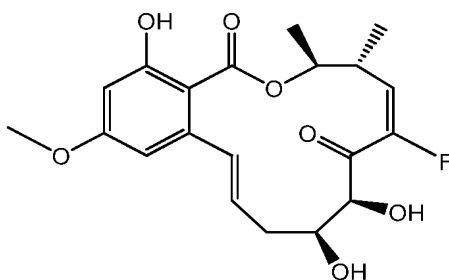
57. (withdrawn) The composition of claim 2, where  $R_8$  and  $R_9$ , taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen.
58. (withdrawn) The composition of claim 2, where  $R_{10}$  is hydroxyl.
59. (withdrawn) The composition of claim 2, where  $R_{11}$  is hydrogen.
60. (withdrawn) The composition of claim 2, where Y and Z together are cyclopropyl.
61. (cancelled)

62. (previously presented) The composition of claim 1 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

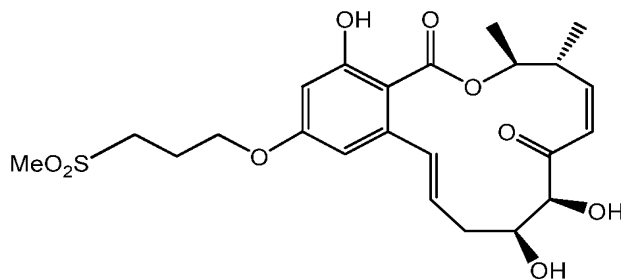
63. (previously presented) The composition of claim 1 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

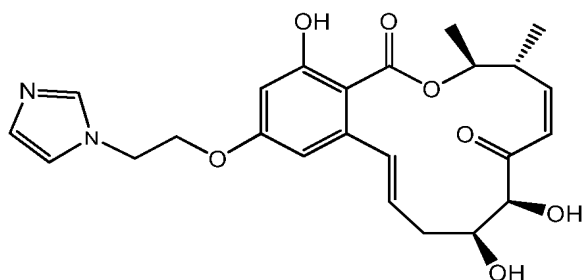
64. (cancelled)

65. (previously presented) The composition of claim 1 wherein the compound has the structure:



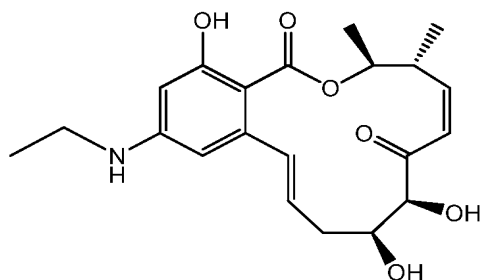
or a pharmaceutically acceptable salt or ester thereof.

66. (previously presented) The composition of claim 1 wherein the compound has the structure:



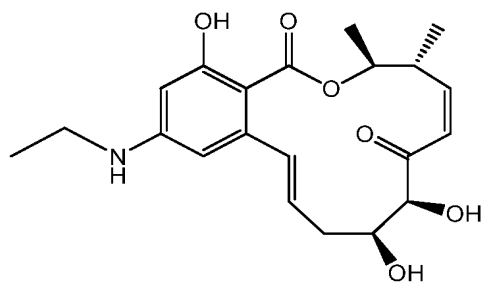
or a pharmaceutically acceptable salt or ester thereof.

67. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



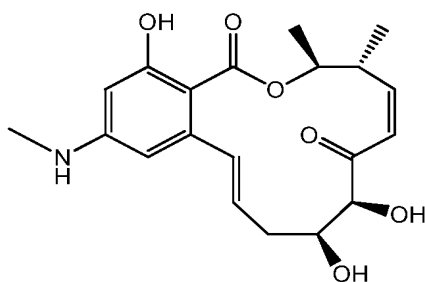
or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

68. (new) The composition of claim 67, having the structure:



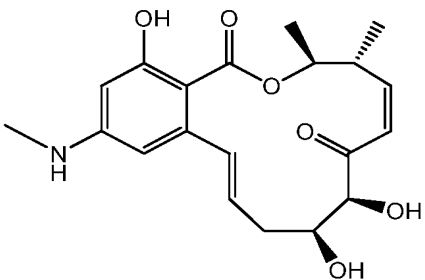


69. (new) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:

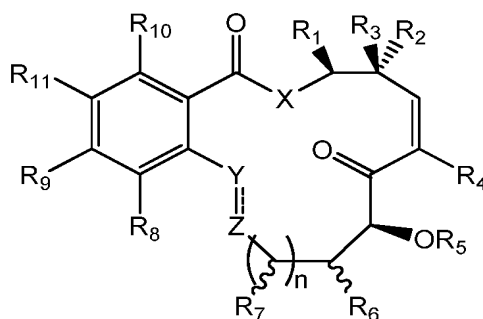


or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

70. (new) The composition of claim 69, having the structure:



71. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester or salt of ester thereof; wherein

R<sub>1</sub> is hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl;

R<sub>2</sub> is C<sub>1-6</sub> alkyl;

R<sub>3</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, or a C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl moiety;  
or

R<sub>1</sub> and R<sub>3</sub>, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R<sub>4</sub> is hydrogen or halogen;

R<sub>5</sub> is hydrogen or an oxygen protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or a C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl or C<sub>2</sub>-C<sub>20</sub> alkynyl moiety optionally substituted with hydroxyl, protected hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;

R<sub>9</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, OR<sub>12</sub>, SR<sub>12</sub>, NR<sub>12</sub>R<sub>13</sub>,

-X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>;

wherein R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, C<sub>2</sub>-C<sub>20</sub> alkenyl, C<sub>2</sub>-C<sub>20</sub> alkynyl, C<sub>1</sub>-C<sub>20</sub> heteroalkyl, C<sub>2</sub>-C<sub>20</sub> heteroalkenyl, C<sub>2</sub>-C<sub>20</sub> heteroalkynyl, C<sub>3</sub>-C<sub>20</sub> cycloalkyl, C<sub>3</sub>-C<sub>20</sub> cycloalkenyl, C<sub>3</sub>-C<sub>20</sub> cycloalkynyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkenyl, C<sub>3</sub>-C<sub>20</sub> heterocycloalkynyl, C<sub>3</sub>-C<sub>14</sub> aryl or C<sub>3</sub>-C<sub>14</sub> heteroaryl; or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X<sub>1</sub> and X<sub>2</sub> are each independently absent, or are oxygen, NH, or

-N(alkyl), or wherein X<sub>2</sub>-R<sub>14</sub> together are N<sub>3</sub> or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

$R_{14}$  is hydrogen, or an  $C_3$ - $C_{14}$  aryl,  $C_3$ - $C_{14}$  heteroaryl,  $C_1$ - $C_{20}$ alkyl( $C_3$ - $C_{14}$ )aryl, or  $C_1$ - $C_{20}$ alkyl( $C_3$ - $C_{14}$ )heteroaryl moiety, or is  $-(C=O)NHR_{15}$ ,  $-(C=O)OR_{15}$ , or  $-(C=O)R_{15}$ , wherein each occurrence of  $R_{15}$  is independently hydrogen,  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl,  $C_2$ - $C_{20}$  alkynyl,  $C_1$ - $C_{20}$  heteroalkyl,  $C_2$ - $C_{20}$  heteroalkenyl,  $C_2$ - $C_{20}$  heteroalkynyl,  $C_3$ - $C_{20}$  cycloalkyl,  $C_3$ - $C_{20}$  cycloalkenyl,  $C_3$ - $C_{20}$  cycloalkynyl,  $C_3$ - $C_{20}$  heterocycloalkyl,  $C_3$ - $C_{20}$  heterocycloalkenyl,  $C_3$ - $C_{20}$  heterocycloalkynyl,  $C_3$ - $C_{14}$  aryl or  $C_3$ - $C_{14}$  heteroaryl; or  $R_{14}$  is  $-SO_2(R_{16})$ , wherein  $R_{16}$  is a  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl or  $C_2$ - $C_{20}$  alkynyl moiety, wherein one or more of  $R_{14}$ ,  $R_{15}$ , or  $R_{16}$  are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

$R_8$  and  $R_9$  may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

$R_{10}$  is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

$R_{11}$  is hydrogen, hydroxyl or protected hydroxyl;

$X$  is O;

$Y$  is  $CHR_{17}$ ,  $C=O$ , or  $CR_{17}$ ; and  $Z$  is  $CHR_{18}$ ,  $C=O$ , or  $CR_{18}$ , wherein each occurrence of  $R_{17}$  and  $R_{18}$  is independently hydrogen,  $C_1$ - $C_{20}$  alkyl,  $C_2$ - $C_{20}$  alkenyl or  $C_2$ - $C_{20}$  alkynyl wherein  $Y$  and  $Z$  may be connected by a single or double bond;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

wherein  $C_3$ - $C_{14}$  heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

72. (new) The composition of claim 71, wherein:

R<sub>1</sub> is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R<sub>2</sub> is methyl;

R<sub>3</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R<sub>1</sub> and R<sub>3</sub>, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R<sub>4</sub> is hydrogen or halogen;

R<sub>5</sub> is hydrogen or a protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;

R<sub>9</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, OR<sub>12</sub>, SR<sub>12</sub>, NR<sub>12</sub>R<sub>13</sub>, -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>, or is lower alkyl optionally substituted with hydroxyl, protected hydroxyl, halogen, amino, protected amino, or -X<sub>1</sub>(CH<sub>2</sub>)<sub>p</sub>X<sub>2</sub>-R<sub>14</sub>;

wherein R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, lower alkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X<sub>1</sub> and X<sub>2</sub> are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X<sub>2</sub>-R<sub>14</sub> together are N<sub>3</sub> or are a saturated or unsaturated heterocyclic moiety, p is 2-10, and

R<sub>14</sub> is hydrogen, or a C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl moiety, or is -(C=O)NHR<sub>15</sub>, -(C=O)OR<sub>15</sub>, or -(C=O)R<sub>15</sub>, wherein each occurrence of R<sub>15</sub> is independently hydrogen, alkyl, heteroalkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or R<sub>14</sub> is -SO<sub>2</sub>(R<sub>16</sub>), wherein R<sub>16</sub> is an alkyl moiety, wherein one or more of R<sub>14</sub>, R<sub>15</sub>, or R<sub>16</sub> are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

R<sub>8</sub> and R<sub>9</sub> may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

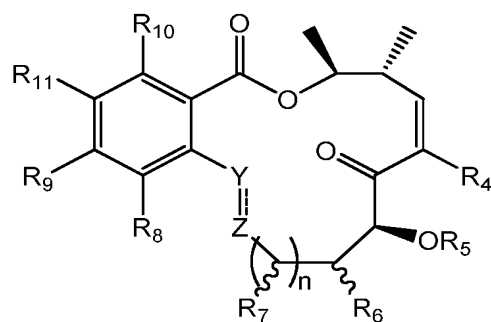
R<sub>10</sub> is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R<sub>11</sub> is hydrogen, hydroxyl or protected hydroxyl;

X is O;

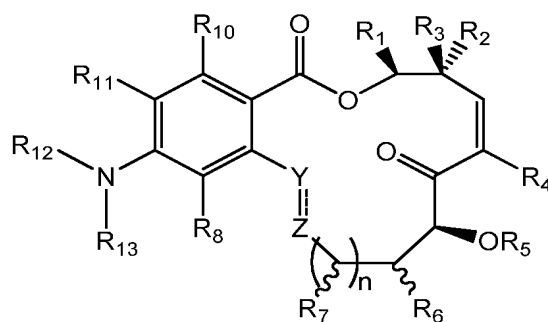
Y is CHR<sub>17</sub>, C=O, or CR<sub>17</sub>; and Z is CHR<sub>18</sub>, C=O, or CR<sub>18</sub>, wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is independently hydrogen or lower alkyl, wherein Y and Z may be connected by a single or double bond.

73. (new) The composition of claim 72, where n is 1.
74. (new) The composition of claim 72, where R<sub>4</sub> is halogen.
75. (new) The composition of claim 72, where R<sub>4</sub> is fluorine.
76. (new) The composition of claim 72, where Y and Z together represent -CH=CH-.
77. (new) The composition of claim 72, where Y and Z together represent trans -CH=CH-.
78. (new) The composition of claim 72, wherein R<sub>1</sub> and R<sub>2</sub> are each methyl and R<sub>3</sub> is hydrogen and the compound has the structure:



wherein  $R_4$ - $R_{11}$ ,  $n$ ,  $Y$  and  $Z$  are as defined in claim 2.

79. (new) The composition of claim 78, wherein  $n$  is 1.
80. (new) The composition of claim 78, wherein  $R_4$  is halogen.
81. (new) The composition of claim 78, wherein  $Y$  and  $Z$  together represent  $-\text{CH}=\text{CH}-$ .
82. (new) The composition of claim 78, wherein  $n$  is 1,  $R_4$  is halogen and  $Y$  and  $Z$  together represent  $-\text{CH}=\text{CH}-$ .
83. (new) The composition of claim 81 or 82 wherein  $-\text{CH}=\text{CH}-$  is trans.
84. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester or salt of ester thereof; wherein

$R_1$  is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or  $\text{C}_3$ - $\text{C}_{14}$  aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl;

R<sub>2</sub> is C<sub>1-6</sub> alkyl;

R<sub>3</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C<sub>3</sub>-C<sub>14</sub> aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or protected hydroxyl; or

R<sub>1</sub> and R<sub>3</sub>, when taken together, may form a saturated or unsaturated cyclic ring of 3 to 8 carbon atoms, optionally substituted with one or more occurrences of halogen;

R<sub>4</sub> is hydrogen or halogen;

R<sub>5</sub> is hydrogen or a protecting group;

R<sub>6</sub> is hydrogen, hydroxyl, or protected hydroxyl;

n is 0-2;

R<sub>7</sub>, for each occurrence, is independently hydrogen, hydroxyl, or protected hydroxyl;

R<sub>8</sub> is hydrogen, halogen, hydroxyl, protected hydroxyl, alkyloxy, or lower alkyl optionally substituted with hydroxyl, protected hydroxyl, SR<sub>12</sub>, or NR<sub>12</sub>R<sub>13</sub>;

R<sub>12</sub> and R<sub>13</sub> are, independently for each occurrence, hydrogen, lower alkyl, C<sub>3</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>14</sub> heteroaryl, alkyl(C<sub>3</sub>-C<sub>14</sub>)aryl, or alkyl(C<sub>3</sub>-C<sub>14</sub>)heteroaryl, or a nitrogen or oxygen protecting group, or R<sub>12</sub> and R<sub>13</sub>, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R<sub>12</sub> and R<sub>13</sub> are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

R<sub>10</sub> is hydrogen, hydroxyl, protected hydroxyl, amino, or protected amino;

R<sub>11</sub> is hydrogen, hydroxyl or protected hydroxyl;

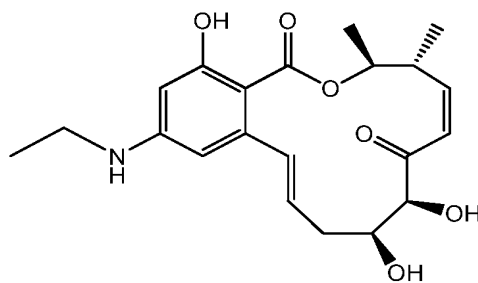
Y is CHR<sub>17</sub>, C=O, or CR<sub>17</sub>; and Z is CHR<sub>18</sub>, C=O, or CR<sub>18</sub>, wherein each occurrence of R<sub>17</sub> and R<sub>18</sub> is independently hydrogen or lower alkyl, wherein Y and Z may be connected by a single or double bond, or

R<sub>13</sub> and R<sub>8</sub> may, when taken together, form a cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl

ether, triethylsilylether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, Troc, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and wherein C<sub>3</sub>-C<sub>14</sub> heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

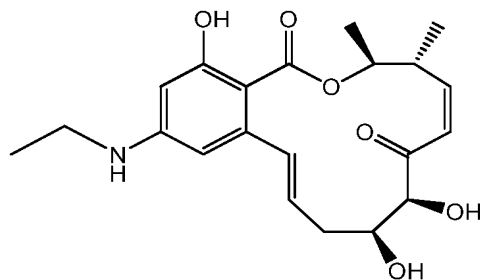
85. (new) The composition of claim 84, wherein n is 1.
86. (new) The composition of claim 84, wherein R<sub>4</sub> is halogen.
87. (new) The composition of claim 84, wherein Y and Z together represent -CH=CH-.
88. (new) The composition of claim 84, wherein R<sub>1</sub> and R<sub>2</sub> are each methyl and R<sub>3</sub> is hydrogen.
89. (new) The composition of claim 84, wherein n is 1, R<sub>1</sub> and R<sub>2</sub> are each methyl, R<sub>3</sub> is hydrogen, R<sub>4</sub> is halogen, and Y and Z together represent -CH=CH-.
90. (new) The composition of claim 87 or 89, wherein -CH=CH- is trans.
91. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



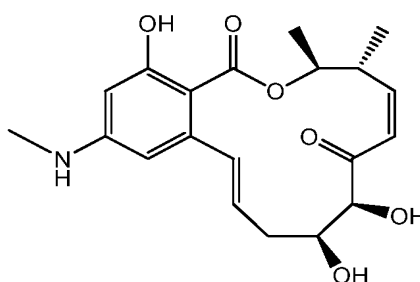
or a pharmaceutically acceptable salt, ester, or salt of ester thereof.



92. (new) The composition of claim 91, having the structure:

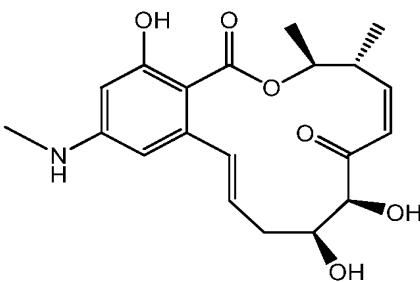


93. (new) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



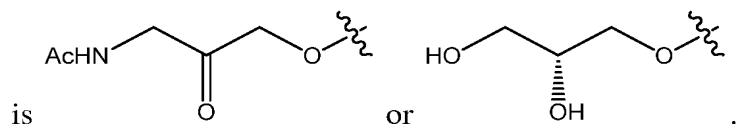
or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

94. (new) The composition of claim 93, having the structure:

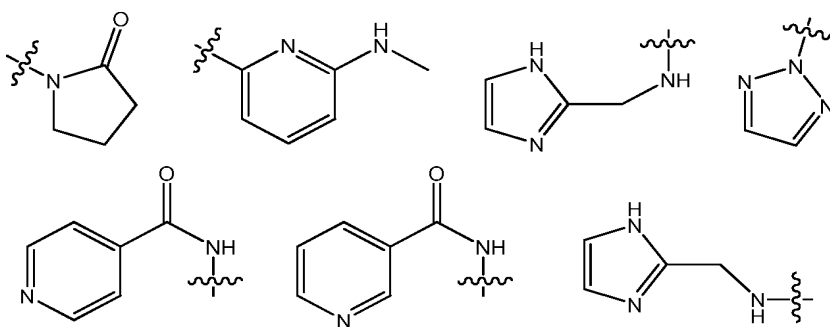


95. (withdrawn-new) The composition of claim 72, where R<sub>1</sub> is hydrogen or methyl.
96. (withdrawn-new) The composition of claim 72, where R<sub>3</sub> is hydrogen or halogen.
97. (withdrawn-new) The composition of claim 72, where R<sub>4</sub> is hydrogen.
98. (withdrawn-new) The composition of claim 72, where R<sub>5</sub> is hydrogen.

99. (withdrawn-new) The composition of claim 72, where  $R_6$  is hydroxyl.
100. (withdrawn-new) The composition of claim 72, where  $R_7$  is hydrogen or hydroxyl.
101. (withdrawn-new) The composition of claim 72, where  $R_8$  is hydrogen or halogen.
102. (withdrawn-new) The composition of claim 72, where  $R_9$  is hydroxyl, protected hydroxyl,  $-OR_{12}$ ,  $-NR_{12}R_{13}$ , or  $-O(CH_2)_pX_2-R_{14}$ , wherein  $R_{12}$ ,  $R_{13}$ ,  $R_{14}$  and  $X_2$  are as defined in claim 2.
103. (withdrawn-new) The composition of claim 102, where  $R_9$  is  $-OR_{12}$ , wherein  $R_{12}$  is methyl, ethyl, propyl, isopropyl, butyl,  $-CH_2COOMe$ , Bn, PMB (MPM), 3,4-CIBn, or  $R_9$



104. (withdrawn-new) The composition of claim 102, where  $R_9$  is  $-NR_{12}R_{13}$ , or wherein  $R_{12}$  is methyl, ethyl, propyl, isopropyl, or butyl, optionally substituted with one or more occurrences of hydroxyl or protected hydroxyl, and  $R_{13}$  is hydrogen or lower alkyl, or  $NR_{12}R_{13}$  together represents a 5- or 6- membered heterocyclic moiety.
105. (withdrawn-new) The composition of claim 102, where  $R_9$  is  $-O(CH_2)_pX_2-R_{14}$ , wherein  $X_2-R_{14}$  together represent  $N_3$ ,  $NMe_2$ ,  $NHAc$ ,  $NHSO_2Me$ ,  $NHCONHMe$ ,  $NHCONHPh$ , morpholine, imidazole, aminopyridine, or any one of:



106. (withdrawn-new) The composition of claim 72, where  $R_8$  and  $R_9$ , taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen

atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen.

107. (withdrawn-new) The composition of claim 72, where  $R_{10}$  is hydroxyl.
108. (withdrawn-new) The composition of claim 72, where  $R_{11}$  is hydrogen.
109. (withdrawn-new) The composition of claim 72, where Y and Z together are cyclopropyl.